

CLAIMS

1. An ion channel modulator molecule (ICMM) derived from a haematophagous arthropod, or a functional equivalent thereof.
2. An ICMM or functional equivalent according to claim 1, which modulates the activity of more than one ion channel simultaneously.
3. An ICMM or functional equivalent according to claim 1 wherein said ion channel(s) is selected from the group consisting of a calcium channel, a potassium channel, a sodium channel, and a sodium-potassium ATPase.
4. An ICMM or functional equivalent according to claim 1 that inhibits the activity of said ion channel(s).
5. An ICMM according to claim 4 that inhibits the activity of said ion channel(s) by binding to said ion channel(s).
6. An ICMM or functional equivalent according to claim 1 which is a vasodilator.
7. An ICMM or functional equivalent according to claim 6 wherein said vasodilation occurs through nitric oxide donation.
8. An ICMM or functional equivalent according to claim 6 which is a vasodilator of coronary vessels.
9. An ICMM or functional equivalent according to claim 6 which is a vasodilator of peripheral vessels.
10. An ICMM or functional equivalent according to claim 1 which does not have a negative inotropic effect.

11. An ICMM or functional equivalent according to claim 1 that has a positive inotropic effect.

12. An ICMM or functional equivalent according to claim 1 that prolongs the action potential of muscle cells.

13. An ICMM or functional equivalent according to claim 12 wherein said muscle cells are cardiomyocyte cells.

14. An ICMM or functional equivalent according to claim 1 which is derived from a haematophagous arthropod including all arthropods that take a blood meal from a suitable host such as insects, ticks, lice, fleas and mites.

15. An ICMM or functional equivalent according to claim 14 wherein said haematophagous arthropod is a horsefly of the *Tabinadae* family.

16. An ICMM or functional equivalent according to claim 15 wherein said horsefly is derived from the *Hybomitra*, *Heptatoma*, *Chrysops*, *Haematopota* or *Tabanus* genera.

17. An ICMM or functional equivalent according to claim 16 wherein said horsefly is *Hybomitra bimaculata*.

18. An ICMM or functional equivalent according to claim 1 comprising the sequence in Figure 9a.

19. An ICMM or functional equivalent according to claim 18 which has greater than 50% identity with the sequence in Figure 9a, preferably greater than 60%, 70%, 80%, 85%, 90%, 95%, 97%, 98% or 99% sequence identity, as defined using the GCG suite of programs (Wisconsin Package Version, 10.1, Genetics Computer Group (GCG), Madison, Wisc.) or the ExPASy (ExpertProtein Analysis System) proteomics server of the Swiss Institute of Bioinformatics.

20. An ICMM or functional equivalent according to claim 1, which is a recombinant protein.

21. An ICMM or functional equivalent according to claim 1, which is genetically or chemically fused to one or more peptides or polypeptides.

22. An ICMM or functional equivalent, according to claim 1, for use in therapy.

23. A nucleic acid molecule encoding an ICMM or functional equivalent according to claim 1.

24. A vector comprising a nucleic acid molecule according to claim 23.

25. A host cell transformed or transfected with a vector of claim 24.

26. A method of preparing an ICMM or functional equivalent, comprising introducing a vector according to claim 24 into a host cell and culturing said host cell under conditions wherein said ICMM or functional equivalent is expressed and recovering said ICMM or functional equivalent.

27. A method of isolating an ICMM or functional equivalent according to claim 1 comprising the steps of:

- a) preparing an extract from a haematophagous arthropod,
- b) separating said extract into fractions containing proteins,
- c) testing said fractions for the ability to modulate ion channel activity
- d) isolating said ICMM or functional equivalent from a fraction that possesses the ability to modulate said ion channel activity.

28. A method according to claim 27 wherein the extract is separated into fractions by fast phase or high performance liquid chromatography, ion exchange chromatography, affinity chromatography, gel filtration or reverse phase high performance liquid chromatography.

29. A method according to claim 27 wherein testing said fractions for the ability to modulate ion channel activity comprises testing for the ability to cause vasodilation and/or positive inotropism and/or lengthen of action potential.

30. A method according to claim 29 wherein testing for the ability to cause vasodilation comprises assessing the effect of the fractions on pre-contracted rat femoral artery rings or assessing the effect of fractions on coronary blood flow in an isolated Langendorf heart.

31. A method according to claim 29 wherein testing for the ability to cause positive inotropism comprises assessing the effect of fractions on whole cell patch clamping in isolated cardiomyocytes or assessing the effect of fraction on left ventricular output in an isolated perfused Langendorf heart.

32. A method according to claim 29 wherein testing for the ability to lengthen action potential comprises assessing the effect of fractions on whole cell patch clamping in isolated cardiomyocytes.

33. An ICMM or functional equivalent obtainable by the method of claim 27.

34. A method according to claim 27 comprising the additional steps of isolating and sequencing the gene encoding said ICMM or functional equivalent.

35. A method of isolating a gene encoding an ICMM or functional equivalent comprising performing the steps recited in claim 27, said method additionally comprising performing the steps of:

- e) obtaining the N-terminal sequence of said isolated ICMM or functional equivalent;
- f) designing a degenerate oligonucleotide; and
- g) using said oligonucleotide to screen a library in order to isolate a gene encoding the ICMM or functional equivalent

36. A pharmaceutical composition comprising a material selected from the group consisting of an ICMM derived from a haematophagous arthropod, or functional equivalent thereof, and a nucleic acid molecule encoding said ICMM or functional equivalent thereof, in conjunction with a pharmaceutically acceptable carrier.

37. A method for the prevention or treatment of a disease or condition caused by a fault in ion channel activity comprising administering to a subject an effective dose of a material selected from the group consisting of an ICMM derived from a haematophagous arthropod, or functional equivalent thereof, a nucleic acid molecule encoding said ICMM or functional equivalent thereof, and a composition according to claim 36.

38. A method according to claim 37 wherein said disease is selected from cardiac conditions such as coronary insufficiency leading to angina, congestive cardiac failure and cardiac arrhythmias; peripheral vascular disease such as cerebro-vascular insufficiency, intermittent claudication and Buerger's disease; vasospastic disorders such as Raynaud's disease, cerebral or coronary vasospasm; reperfusion following stroke and myocardial infarction; shock including septic shock, haemorrhagic shock and cardiogenic shock; hypertension; to assist in circulatory support during and following cardio-pulmonary by-pass or angioplasty procedures.

39. A process for the formulation of a composition according to claim 36 comprising bringing said ICMM or functional equivalent, or said nucleic acid molecule, into association with a pharmaceutically acceptable carrier or adjuvant.

40. A method for studying the effect of ion channel modulation, including vasodilation, inotropism and lengthening of action potential, *in vitro* comprising administering to a cell or an organ an ICMM or functional equivalent according to claim 1.

41. An ion channel modulator comprising a polypeptide or peptide having the sequence psggrrs.

42. An ion channel modulator comprising a Kazal type protein.

43. The ion channel modulator of either of claims 41 or 42, wherein said ion channel is selected from the group comprising a sodium channel, a potassium channel, a calcium channel or a sodium-potassium ATPase.
44. The ion channel modulator of either of claims 41 or 42, wherein said ion channel modulator is a vasodilator.
45. A method for treating or preventing a disease or condition caused by a fault in ion channel activity, comprising administering a therapeutically effective amount of a medicament, said medicament comprising a polypeptide or peptide having the sequence psggrs, and a Kazal type protein.
46. A pharmaceutical composition comprising a peptide or polypeptide as recited in claim 42 in combination with a pharmaceutically acceptable carrier.
47. A method for studying ion channel modulation *in vitro* comprising administering to a cell or an organ a peptide, polypeptide or Kazal type protein as recited in either of claims 41 or 42.